

# Sleep-related breathing disorders · 1

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## Obstructive sleep apnoea: definitions, epidemiology, and natural history

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Definitions, epidemiology, and the natural history of obstructive sleep apnoea (OSA) are usefully considered together. This is because OSA is not a condition that one either has or does not have, but it exists in a continuum between complete normality through to gross, all night, obstructive sleep apnoea. Thus, the prevalence of the condition depends critically upon definitions and where one draws the arbitrary line between normality and abnormality. A further complication is that, particularly in the mid range of severity, there is considerable night to night variation.<sup>1</sup> As with systemic hypertension, it is probably not very useful to try to define a threshold for normality, but rather to accept that a continuum exists and quote prevalences for various levels of "sleep apnoea activity". This should allow correlations with symptoms and secondary consequences to be drawn, and an attempt made to calculate risk/benefit ratios for various treatments at these different "sleep apnoea activity" levels – again, similar to the approach in systemic hypertension. This, or course, supposes that we know exactly how to measure "sleep apnoea activity" (as well as its main consequences, sleep fragmentation) but, as we discuss later, we do not.

### Aetiology

At sleep onset all skeletal muscle loses tone. This is probably necessary to sleep comfortably. The pharyngeal muscles that dilate and maintain patency in the upper airway share in this general loss of muscle tone so that even in totally normal, non-snoring, individuals there is narrowing of the upper airway<sup>2</sup> with an increase in airways resistance (fig 1). This narrowing at sleep onset varies considerably between individuals and, when occurring beyond a certain degree, the pharyngeal walls come close enough together (with or without the uvula within the lumen) to generate snoring. Further narrowing allows complete collapse, hence the term "sleep apnoea". Although the degree of narrowing is a continuous variable, the onset of snoring and of complete collapse are clearly two "steps" in the process which have been seized on as easily defined and measured consequences. So dramatic is the point of onset of apnoeas that initially these were

believed to be the primary (and only) pathological event.<sup>3</sup> An early definition of the sleep apnoea syndrome required the counting of these apnoeas, and >5/hour of >10 second apnoeas was an early popular example.<sup>3</sup> The choice of >5/hour and of >10 second duration was almost entirely arbitrary, but some definitions were needed in the early days to facilitate research in this area. The recognition of hypopnoeas as arousing events<sup>4</sup> required the addition of some definition of these events too. Definitions of hypopnoeas are less universal than those for apnoea. Sometimes a 50% reduction in ribcage and abdominal excursion for 10 seconds is required, the 10 second requirement may or may not be abandoned if a dip of >3% or >4% in  $\text{Sao}_2$  accompanies it, and the calculation of the preceding baseline varies between laboratories as well. These rigid definitions have now largely outlived their clinical usefulness<sup>5</sup> because of the recognition of sleep disturbance from upper airways narrowing, even without hypopnoea or hypoxaemia – a point to which we will return. This might imply that the real requirement is to measure short arousals from the EEG but, despite attempts to define arbitrarily such arousals,<sup>6</sup> there is no useful recognised stand-

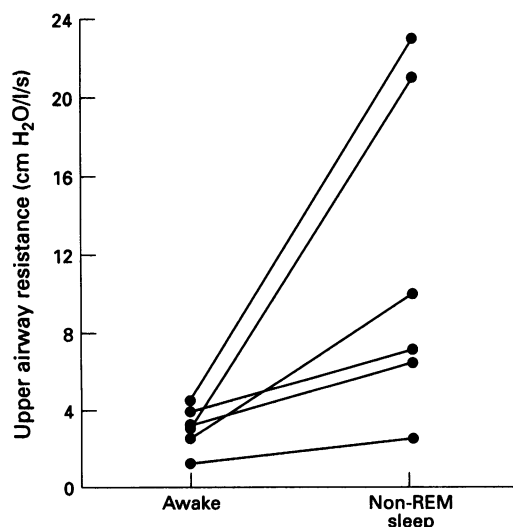


Figure 1 Changes in upper airways resistance with the onset of non-REM sleep in six normal, non-snoring, subjects. Note the considerable interindividual variability. Redrawn from Wiegand et al.<sup>2</sup>

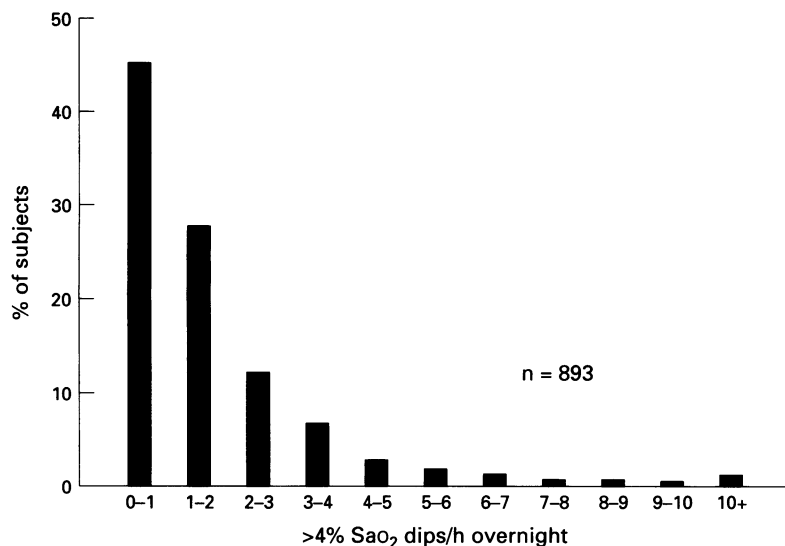


Figure 2 Distribution of overnight hypoxic dipping rates in 893 randomly selected men aged 35–65 years. Redrawn from Stradling and Crosby.<sup>15</sup>

ard. This is because we do not know what aspect of sleep disturbance is responsible for daytime symptoms – for example, is a 10 second arousal equivalent to two five second arousals, and is the quality or depth of the interarousal sleep more important than the actual arousals? There are even suggestions that cardiovascular markers of arousal might be at least as informative as those based on the EEG.<sup>7,8</sup>

The factors that tend to enhance the degree of upper airways narrowing with sleep onset are those that (a) narrow the pharynx to start with, and (b) dynamically load the airway from outside and overwhelm the pharyngeal dilators as tone is withdrawn. For example, residual tonsils, retrognathia, or external pressure from neck obesity<sup>9</sup> will cause structural narrowing of the pharynx, present even when awake. A smaller starting size means that the normal withdrawal of dilator tone will produce a significantly greater increase in pharyngeal airways resistance. Neck obesity will also load the pharyngeal muscles, which may be able to cope when awake (by increasing their activity<sup>10</sup>) but fail when tone is withdrawn at sleep onset. The concurrence of more than one of these factors, such as obesity and retrognathia or tonsillar hypertrophy, may be particularly potent at provoking sleep-related collapse of the upper airways.

### Epidemiological studies

The early epidemiological studies had to use the then current definitions of sleep apnoea referred to above. The study by Lavie<sup>11</sup> was the first attempt at a random survey of people in the community. A questionnaire on sleep-related problems was returned by 1502 industrial workers, from which 300 men were selected in proportions equal to the reported prevalence of excessive sleepiness (8.1%), insomnia (20.1%), and no complaints (71.8%), and asked to attend for conventional hospital polysomnography (without oximetry monitoring). Eighty per cent of the “sleepy” group

and 19% of the “no complaints” group agreed to the study, with the overall acceptance being 78/300 (26%). Seven of the 20 in the “sleepy” group, one of the 17 in the “insomnia” group, and three in the 41 “no complaints” group had more than 10 apnoeas per hour (apnoea index, AI). Thus, 11 of the original 300 had AI values of >10, but three had symptomless central apnoeas of questionable significance. Hence, eight out of 300 (2.7%) is the estimate of AI values >10/hour from this study. Because of the problems of bias which affected who agreed to take part in the sleep studies, it is hard to extrapolate backwards to the original population.

Berry *et al*<sup>12</sup> studied 46 heavily snoring men over 30 years of age in the sleep laboratory, recruited via newspaper advertisements. Six had AI values of >5/hour and, if it is assumed that 10% of men are heavy snorers, this gives a population estimate of 1.3%.

Gislason *et al*<sup>13</sup> posted questionnaires to 4064 randomly selected men aged 30–69 years, receiving back 3201 (80%). Based on the answers, 166 with the highest ratings for sleepiness and snoring were selected for laboratory study, of whom 61 agreed to be studied. Apnoeas and hypopnoeas were measured (apnoea/hypopnoea index, AHI); 16 had AHI values of >5/hour and 10 had AHI values of >10/hour. If one assumes that the questionnaire identified all the likely sufferers, then extrapolating backwards gives overall prevalence estimates of 1.4% and 0.9% for AHIs of 5 and 10/hour respectively. However, it is very unlikely that all such individuals were included in the highest sleepiness/snoring categories so that these represent underestimates.

Cirignotta *et al*<sup>14</sup> posted questionnaires to 3479 men aged 30–69 years. Of the 1170 returning the questionnaire (34%), 119 said they snored every night and 40 were admitted for polysomnography. Thirteen had an AI of >10/hour and 20 of >5/hour. Again, making certain assumptions, this extrapolates back to give overall prevalence estimates of 5.1% and 3.3% for AI values of 5 and 10/hour, respectively; only two (0.5%) had severe symptomatic OSA requiring treatment.

From the above it will be clear that such studies are bedevilled by problems of bias in the sampling, and of not being sure if techniques to extract a high risk subgroup for further study are particularly sensitive or specific.

Because of these problems and the expense of hospital polysomnography, we tried to perform a limited sleep study (overnight oximetry at home) on the whole of a selected population of 1001 men aged 35–65 years.<sup>15</sup> At the time it was believed that most OSA-related events would produce measurable dips in arterial oxygen saturation (Sao<sub>2</sub>). Of the 1001 selected, 893 agreed to overnight oximetry. Only 0.3% had severe (>20/hour >4% dips in Sao<sub>2</sub>) and symptomatic OSA, 1% had >10/hour and 4.6% had >5/hour. The distribution of severity of overnight hypoxic dipping was like half a Gaussian curve and did not suggest a bimodal distribution (fig 2). An approximate overall estimate of the prevalence of different levels

Prevalence studies on sleep apnoea

Author	Reference	Country	Population	Age range	Method	Criteria	Estimated whole population prevalence	
Franceschi <i>et al</i> (1982)	44	Italy	2518 consecutive hospital admissions M and F	6–92	(1) Questionnaire (2) Polysomnography on subgroup of 87 (no oximetry)	AI >10/h	1%	
Lavie (1983)	11	Israel	1262 M	Working age	(1) Questionnaire (2) Polysomnography on 78 (no oximetry)	AI >10/h AI >10/h	2.7% 0.7%	
Berry <i>et al</i> (1986)	12	USA	60 heavy snorers	30–?	(1) Newspaper advert recruitment (2) Polysomnography on 46	AHI >5/h	?1.3%	
Telakivi <i>et al</i> (1987)	45	Finland	Approximately 278 M	41–50	(1) Part of a twin study (2) 25 snorers and 27 non-snorers had polysomnography	AHI >20/h >10/h >4% Sao <sub>2</sub> dips	0.4% 1.4%	
Gislason <i>et al</i> (1988)	13	Sweden	3100 M	30–69	(1) Questionnaire (2) 61 sleep snorers had polysomnography	AHI >10/h AHI >5/h	0.9% 1.4%	
Cirignotta and Lugaesi (1989)	14 and 33	Italy	1170 M	30–69	(1) Questionnaire (2) 40 heavy snorers had polysomnography	Severe and symptomatic AHI >10/h AHI >5/h	0.5% 3.3% 5.1%	
Stradling (1991)	15	UK	1001 M	35–65	Oximetry on 893	Severe, symptomatic and >20/h >4% Sao <sub>2</sub> dips >10/h >4% Sao <sub>2</sub> dips >5/h >4% Sao <sub>2</sub> dips	0.3% 1% 4.6%	
Gleadhill <i>et al</i> (1991)	46	Northern Ireland	920 M	40–64	(1) Questionnaire (2) Oximetry on: 138 “symptomatic” 164 “controls”	>10/h >3% Sao <sub>2</sub> dips + symptoms	0.8%	
Young <i>et al</i> (1993)	21	USA	1670 M 1843 F	30–60	(1) Questionnaire (2) 605 had polysomnography	AHI ≥ 15/h AHI ≥ 10/h AHI ≥ 5/h AHI ≥ 15/h AHI ≥ 10/h AHI ≥ 5/h	9% 15% 24% 4% 5% 9%	
Approximate average (not including last row)						>20 events/h >10 events/h > 5 events/h	0.3–0.7% 0.8–3% 1.5–5%	

of “sleep apnoea activity” in these and other studies is listed in the table.

In the course of our study it was clear that there were complaints of sleepiness in the presence of normal overnight oximetry traces. About this time it was beginning to be suspected that heavy snoring alone might lead to sleep disruption with apnoeas, hypopnoeas, or even significant hypoxic dips. We looked at this<sup>16</sup> and could confirm the marked association between sleepiness and snoring that could not be accounted for by co-correlates such as alcohol consumption, obesity, or conventional OSA (as measured by hypoxic dips). Indeed, it seemed that there might be more excessive sleepiness in our study population due to snoring alone than due to conventional OSA.

Recently Guilleminault *et al*<sup>17,18</sup> have clearly shown that arousal from sleep can be repeatedly provoked by increases in upper airways resistance in the absence of apnoeas, hypopnoeas, hypoxic dips, and possibly sometimes even without snoring (fig 3). This is because it is likely that the usual arousal stimulus is the compensatory increase in ventilatory effort in response to the obstruction rather than blood gas disturbances.<sup>19,20</sup> Heavy snorers can generate pleural pressure swings (as large as –80 cm H<sub>2</sub>O) which are vastly in excess of those that will wake normal subjects (approximately –10 to –20 cm H<sub>2</sub>O).

This means that all the prevalence studies done to date have not looked at *all* the path-

ological events involving upper airways narrowing during sleep that can lead to recurrent arousals and daytime symptoms of sleepiness; they have probably only registered the tip of the iceberg, albeit the most severe end of the spectrum. Even the most recent and comprehensive polysomnographic prevalence study of OSA in men and women<sup>21</sup> has failed to include these symptomatic patients with what has been variously called the “upper airways resistance syndrome”, “snoring-induced arousals”, or “crescendo snoring” (this last term because one of the patterns is increasingly loud snoring terminated by arousal). Young *et al* found an extraordinarily high prevalence of sleep apnoea in an apparently healthy population, somewhat greater than previous studies.<sup>21</sup> The authors started with 4284 questionnaires sent to men and women aged 30–60 years of whom 3513 (82%) were returned. Of these, 1453 were approached by telephone and invited to attend for laboratory polysomnography. These 1453 consisted of all subjects reporting habitual snoring (28% of women and 44% of men), and a 25% random sample of subjects who were not habitual snorers. Of these 1453, 625 agreed to be studied and 605 had analysable tracings. The sleep study data were analysed for respiratory events (apnoeas of >10 seconds and hypopnoeas were defined as any reduction in air flow with >4% dip in Sao<sub>2</sub>). Repeat studies were done on 40 subjects which showed similar mean results,

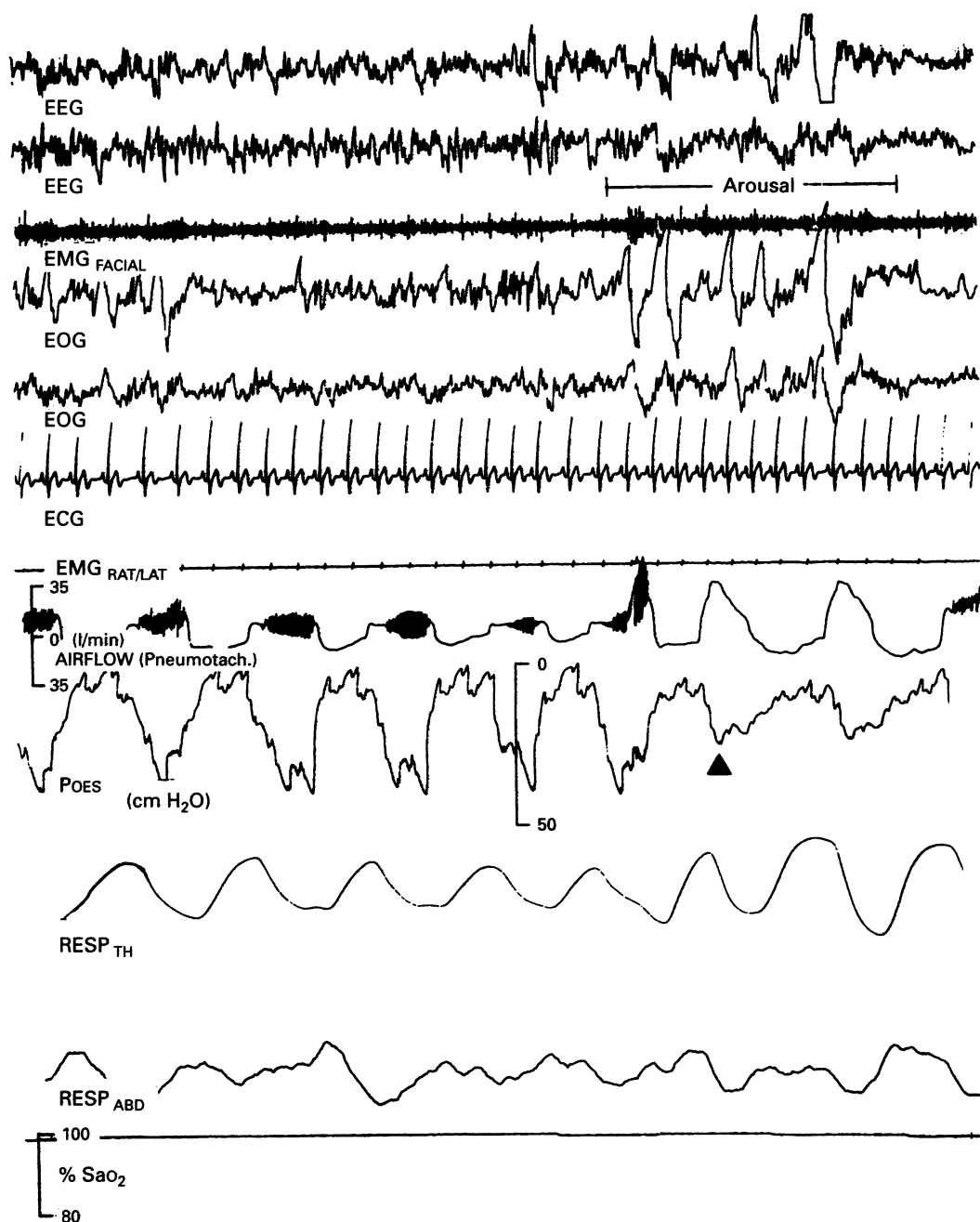


Figure 3 Tracings of one snoring-induced arousal. Note the snoring being picked up on the flow limited airflow tracing and big inspiratory efforts shown on the oesophageal pressure tracing (POES) falling as low as  $-40$  cm  $H_2O$ . Just before the filled triangle (POES tracing) the snorer wakes with a sudden increase in inspiratory flow and a reduction of the oesophageal pressure swings. There is very little hypoventilation and no hypoxaemia.  $EMG_{RAT/LAT}$  = leg electrodes;  $RESP_{TH}$  = ribcage movement;  $RESP_{ABD}$  = abdominal movement. From Guilleminault et al.

but there is no information on how many subjects crossed their AHI thresholds between the two studies. Hypersomnolence was assessed using three questions (excessive daytime sleepiness, waking unrefreshed, uncontrollable sleepiness that interferes with life) answered on a five-point scale. Responses 4 and 5, frequent or habitual ( $\geq 2$  days per week), were deemed hypersomnolent.

Extrapolating back to the original population gave estimated prevalences for  $AHI \geq 5$ ,  $\geq 10$ , and  $\geq 15$  of 9%, 5% and 4% for women and 24%, 15% and 9% for men. The difference in prevalence between men and women is considerably less than is seen in sleep clinics. The definition of a respiratory event did not differ-

entiate between central or obstructive apnoea (or whether there was an associated arousal). Laboratory polysomnography, particularly in non-hypersomnolent subjects, does disturb sleep producing increasing amounts of fluctuating and lighter sleep during which periodic breathing is more common. In addition, full polysomnography in our experience encourages people to lie on their backs more than usual (when obstructive events are most common). Interestingly, the presence or absence of snoring was only predictive of AHI values  $>15$ , perhaps suggesting that AHI values less than this may have been made up of a significant proportion of subjects with central apnoeas due to disturbed sleep.

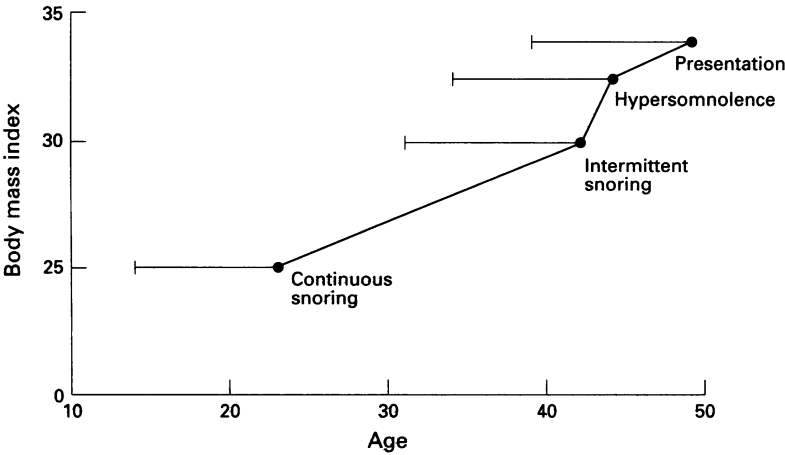


Figure 4 Evolution of symptomatic obstructive sleep apnoea as age and weight increase. Retrospective survey of 118 patients. Error bars are SD. Redrawn from Lugaresi et al.<sup>33</sup>

Hypersomnolence by their definition was also common, higher in women than men. In men the presence of excessive daytime sleepiness ( $\geq 2$  days/week) was 7% in subjects with no sleep-disordered breathing, 23% in habitual snorers (AHI  $< 5$ ), and 22% in those with AHI  $\geq 5$ . This indicated that reported snoring was just as predictive of sleepiness as the sleep study result, a phenomenon observed by others.<sup>12 22–26</sup>

The authors decided to combine AHI and hypersomnolence into a definition of “sleep apnoea syndrome” to give the final prevalences shown in the table. This approach implies that a considerable number of men (83%) with an AHI of  $\geq 5$  (and 75% with AHI of  $\geq 15$ ) appear to have no significant symptoms. Conversely, 91% of hypersomnolent women have an AHI of  $< 5$ . This makes it harder to accept that when hypersomnolence and higher AHI values occur in the same individual the two are necessarily connected, other than by chance. It needs stressing that in this situation we are considering a community population and not patients in a sleep clinic.

The complexities in the interpretation of this large and detailed study further indicate how

difficult it is to identify individuals in a population who have the clinical syndrome and would benefit from treatment. One is forced to conclude that the available epidemiological studies are inadequate to estimate the true prevalence of symptomatic sleep disturbance due to excessive upper airways narrowing during sleep. It has been suggested that the proper assessment of this condition now needs an oesophageal balloon (to measure increases in ventilatory effort) and detailed analysis of the EEG (to document all the arousals that terminate obstructive events, which are often as short as five seconds or less). This is financially impossible in most clinical sleep laboratories and clearly out of the question for an epidemiological study. However, there are alternative ways of inferring both increased ventilatory effort – for example, ribcage/abdominal paradox, snoring, pulsus paradox,<sup>27</sup> and the ballistocardiogram<sup>28</sup> – as well as sleep disturbance – for example, body movements,<sup>29</sup> increases in heart rate and blood pressure,<sup>7 8</sup> and other autonomic variables.<sup>30</sup> The measurement of some of these simpler variables should be adaptable for home use in large epidemiological studies. If the derivatives from such devices can be correlated with validated and simple measures of daytime sleepiness such as the Epworth sleepiness scale,<sup>31 32</sup> then such data would put us considerably further forward in establishing the true health burden of this relatively new and increasingly complex syndrome.

### Natural history of OSA

At presentation to the sleep clinic it is usually clear that the symptom of daytime sleepiness has been coming on over several years. In addition, there is usually a very long history of snoring for 10 years or more. Indeed, a relatively acute onset makes one look for a more specific cause of OSA such as hypothyroidism.

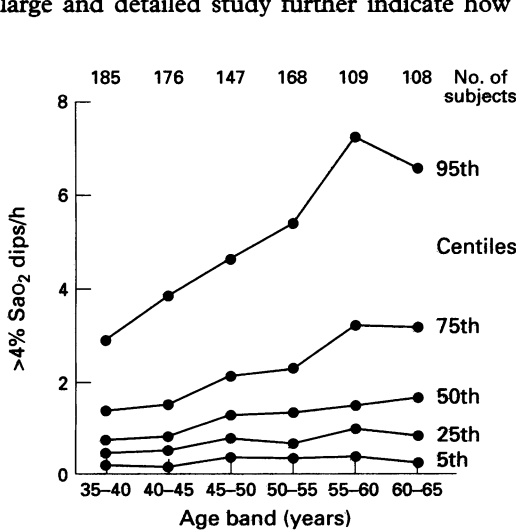


Figure 5 Relation between age and hypoxic dipping overnight in 893 randomly selected men. In the older age range there is a tail of higher rates of hypoxic dipping (the 95th centile of the dip rate more than doubling across the age range). Numbers of subjects in each group are shown at the top of the graph. Redrawn from Stradling.<sup>5</sup>

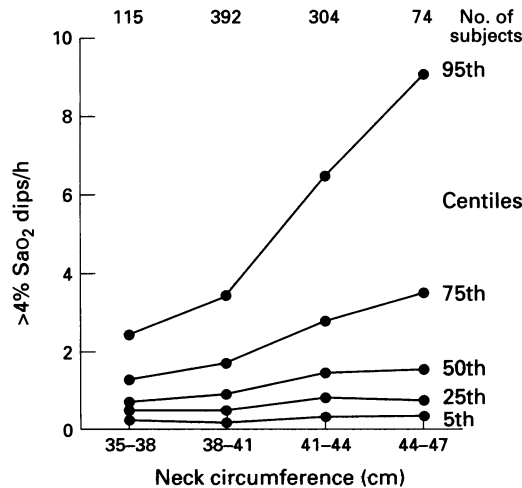


Figure 6 Relation between neck circumference and hypoxic dipping overnight in 893 randomly selected men aged 35–65 years. In the group with larger neck circumferences there is a tail of higher rates of hypoxic dipping (the 95th centile of the dip rate almost quadrupling across the neck circumference range). Numbers of subjects in each group are shown at the top of the graph. Redrawn from Stradling.<sup>5</sup>

In a retrospective study Lugaresi *et al*<sup>33</sup> closely questioned 118 patients with OSA about their past symptoms and body weights. Figure 4 shows the evolution from just snoring when younger and lighter, to OSA when older and heavier. Both increasing age and body weight are independent risk factors for developing snoring and OSA. In our cross sectional epidemiology study of a randomly selected population,<sup>15</sup> age and neck circumference (a simple measure of neck obesity) were also significant predictors of sleep apnoea prevalence (figs 5 and 6). The epidemiology study of Young *et al*<sup>21</sup> also found neck circumference to be the best predictor of AHI.

Guilleminault<sup>34</sup> has suggested other factors, occurring much earlier in life, that may contribute to the evolution of OSA when older. As mentioned earlier, retrognathia or micrognathia is a risk factor for the development of excessive narrowing of the pharyngeal airway during sleep. There is some evidence that lower facial shape may to some extent be inherited and account for some of the familial aggregation of sleep apnoea and snoring,<sup>35,36</sup> particularly in the non-obese (P Jennum, personal communication). In addition to this genetic control, there is the possibility that other factors influence growth of the lower jaw. It has been known for a long time that adenoidal enlargement can influence the development of the lower face and jaw, probably by provoking mouth breathing.<sup>37,38</sup> The "adenoidal facies" is the familiar clinical term for increased anterior face height in the lower third of the facial skeleton, steep mandibular plane and an associated class II occlusion or overjet. Following adenoidectomy at an early enough age, there is some evidence that these abnormalities may resolve to some extent.<sup>39</sup> Enlarged tonsils may retard facial growth as well.<sup>40</sup> Primate experiments where the nose is plugged at birth show that considerable deformity and underdevelopment of the lower jaw will result.<sup>41</sup>

This work has led to the hypothesis that adenoidal, and perhaps tonsillar, enlargement in the infant may provoke hypoplasia of the lower jaw. The skeletal changes are similar to those seen in some patients with sleep apnoea (particularly the less obese),<sup>42,43</sup> and thus some of the seeds of adult sleep apnoea may be sown early in childhood.

No proper longitudinal studies exist to allow one to properly dissect out the evolving factors that together determine the degree of upper airways narrowing during sleep. Not all obese patients snore or have sleep apnoea, and not all patients with sleep apnoea are obese. It is our view that lower facial structure is just one of the variables (along with, for example, age, pharyngeal size, tonsillar size) that determine how sensitive one is to the effects of increasing weight. If any of these factors is particularly bad, it alone may cause sleep apnoea.

### Conclusions

The prevalence of sleep apnoea, measured using conventional indices (apnoea, hypopnoea, hypoxic dips), has been fairly well es-

tablished in a number of studies. However, these conventional indices fail to document subjects with significant, symptomatic sleep disturbance due to obstructive snoring but without apnoeas, hypopnoeas, or hypoxic dips. The true health burden of this syndrome is therefore not clear, but is likely to be over 1% of middle aged men. The dominant factors that will affect prevalence in any particular population are the age structure and obesity distribution. The occurrence in early life of adenoidal enlargement may also influence the later prevalence of sleep apnoea and snoring through alterations to the shape of the lower face.

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